BIOGRAPHICAL SKETCH

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NAME	POSITION TITLE
Fisher, Nicole M.	Graduate Student
eRA COMMONS USER NAME fishenm1	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
Miami University, Oxford OH	BS	2010-2014	Biochemistry
Vanderbilt University, Nashville TN	PhD	2014-present	Pharmacology

A. Personal Statement

I am a graduate student in the Department of Pharmacology at Vanderbilt University with a strong interest in the molecular mechanisms of neurological disease. While earning my undergraduate degree in biochemistry at Miami University, I performed research aimed at understanding the role of cohesin complex proteins in the cell cycle and developed a strong foundation in molecular biology. I also completed coursework outside of my major in neurophysiology and psychopharmacology. These courses reaffirmed my passion for neurobiology and drove me to pursue my current position as a graduate student in the labs of Colleen Niswender and Jeff Conn. The focus of my graduate work is to investigate the therapeutic potential of allosteric modulators of metabotropic glutamate receptor 7 ($mGlu_7$) in mouse models of Rett Syndrome and *MECP2* Duplication Syndrome.

B. Positions and Honors

Honors and Awards

2010- 2014	Margaret Barr Amos Grant
	Miami University Bridges Program
	Miami Resident Scholarship
	Wilson Sporting Goods Company Scholarship
2012-2014	John H. Buckingham Scholarship
2013-2014	Dean's Scholar Undergraduate Research Award
2014-present	Phi Beta Kappa
2015-present	NIH Training Grant in Pharmacological Sciences

Professional Memberships

2012-2014	American Chemical Society
2015-present	Society for Neuroscience

C. Contribution to Science

Characterization of the role of cohesin complex proteins in the cell cycle

Cohesin complexes hold sister chromatids together during metaphase and mediate proper dissociation at the initiation of anaphase. Additionally, they have been shown to play important roles in DNA repair and transcription. During my undergraduate work, I used RNA interference to knock down expression of the alpha-kleisin SYN3 in the plant model, *Arabidopsis thaliana*. Reduction of SYN3 during meiosis resulted in defects in chromosome synapsis and synaptonemal complex formation. Reduction of SYN3 also altered transcript levels of other genes known to be involved in meiotic recombination. This suggests a role for SYN3 in gene transcription, possibly by mediating long-range chromatin interactions. Beyond deepening our current understanding of the cell cycle, the study of cohesin complexes has clinical relevance as well. Cornelia de

Lange Syndrome, for example, is caused by mutations in either SMC1A or SMC3 and results in severe impairments in physical and intellectual development. Mutations in cohesins have also been reported in various forms of cancer. Thus, a more complete understanding of cohesin complexes may drive the development of novel therapeutics for cancer and developmental disorders.

1. Yuan L, Yang X, Ellis JL, Fisher NM, Makaroff CA. (2012) The Arabidopsis SYN3 cohesin protein is important for early meiotic events. *Plant J.* 7(1): 147-60.

Exploration of $mGlu_7$ as a therapeutic target for the treatment of MeCP2-related disorders

Rett Syndrome is a devastating neurodevelopmental disorder with an incidence of about 1 in every 1000 female births. Girls with Rett Syndrome develop normally for 6-18 months, but then undergo rapid developmental regression in which they lose acquired speech, social skills, and purposeful use of their hands. They develop autistic-like features, motor abnormalities, seizures and apneas. It was discovered that Rett Syndrome is caused by mutations in the transcription factor methyl-CpG-binding protein 2 (MeCP2). More recently, it has come to light that cases of male intellectual disability can be explained by duplication of the *MECP2* locus. Thus, the correct dosage of MeCP2 is critical for proper brain function.

The Niswender lab has found that $mGlu_7$ mRNA and protein levels are significantly reduced in Mecp2 knockout mice. Moreover, a positive allosteric modulator of $mGlu_7$ has been observed to rescue deficits in long-term potentiation at the Shaffer collateral-CA1 synapse in the hippocampus along with deficits in a conditioned fear behavioral paradigm. In my graduate work, I plan to further explore the potential of $mGlu_7$ compounds to treat other symptoms of Rett Syndrome and to explore the possibly that $mGlu_7$ compounds might also be efficacious in a mouse model of *MECP2* Duplication Syndrome.